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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,229	12/07/2001	Junming Le	0975.1005-014	8474

21005 7590 03/24/2006

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,229	LE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-10,12-14,16,17,19,20 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7-10,12-14,16,17,19,20 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 12/29/06 has been entered.

Applicant's amendment, filed 12/29/06, has been entered.
Claims 11, 15, 18 and 21 have been canceled. Claims 2 and 6 have been canceled previously.
Claims 1, 3-5, 7-8 and 14 have been amended
Claim 22 has been added.

Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 are pending.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Action will be in response to applicant's arguments, filed 12/29/06.

3. Applicant's assertions concerning priority of the instant application have been fully considered but are not found convincing essentially for the reasons of record as they apply to the recitation of "TNF-α-mediated human neoplastic disease".

Applicant relies upon "TNF-α-related human diseases", including "acute and chronic diseases" and "neoplastic disease", which is characterized as a disease or condition associated with levels of a substance reactive with an anti-TNF antibody to support the recitation of "TNF-α-mediated neoplastic disease", as currently claimed.

Also, the cytokine TNF-α may be related to certain tumors or may be expressed / secreted by certain tumors, neoplastic disease are due to a number of causative agents and etiologies but not mediated or transmitted by TNF-α.

Also, see the rejections under 35 USC 112, first paragraph, new matter and enablement below.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species to represent the entire genus of "TNF-α-mediated neoplastic diseases", as currently claimed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, reliance upon the genus of "TNF-α-mediated / related human diseases" and the disclosure of "malignant diseases involving TNF-secreting tumors" (see (E) malignant pathologies including ... under the heading of TNF-related pathologies on page 59 of the instant specification) does not provide sufficient written description for "TNF-α-mediated neoplastic diseases", as currently claimed.

Also it is noted that the earliest priority application USSN 07/670,827, filed 3/18/91, simply discloses "malignant diseases involving TNF-secreting tumors" in the context of as "a disease or condition associated with levels of a substance reactive with an anti-TNF antibody",
while subsequent priority USSNs describe "TNF-secreting tumors or other malignancies involving TNF, such as chronic lymphocytic and/or myelodysplastic syndrome and lymphomas".

Therefore, the written description of defining TNF-related malignancies has changed in the family of priority documents for this application.

Also, with respect to claims 7-10, it is noted that "wherein said anti-TNF chimeric antibody comprises a non-human variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 3, 4 and/or 5" would appear, at best, to receive a priority date back to USSN 08/192,093, filed 2/4/94 (now U.S. Patent No. 6,284,471).

Given the number of continuation-in-part applications, applicant is invited to clarify the support under 35 USC 112, first paragraph, for the priority of the instant claims in the lineage of priority documents for establishing the record for clarity.

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Neither the priority applications nor the instant application have provides a sufficient description of a representative number of species to represent the entire genus of "TNF-mediated neoplastic diseases", as currently claimed.

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Applicant is reminded that priority and written description differ from prior art determinations.

Also, applicant is reminded that a species reads on a genus.

Again, if applicant desires priority prior to the instant application, applicant is invited to point out and provide documentary support for the priority of the instant claims.

Applicant is invited to consider whether support for claims drawn to "treating TNF-secreting tumors" can be supported by the written description of the instant and priority applications and whether the ordinary artisan could attribute a reasonable interpretation of the metes and bounds or scope of said "TNF-secreting tumors" at the time the invention was made.

4. Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 1, 3-5 and 7-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 1, 3-5 and 7-21 are indefinite in the recitation of "cA2" because its characteristics are not known. The use of "cA2" monoclonal antibody as the sole means of identifying the claimed antibody renders the claim indefinite because "cA2" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct hybridomas / cell lines.

Applicant's reliance upon amending the claims to recite the variable region of monoclonal antibody A2 and binding characteristics are acknowledged.

However, the designation cA2 refers to a particular biological material and it is not defined completely by the variable domain of its parent antibody molecule and functional characteristics.

Therefore, the metes and bounds of the claimed cA2 antibody are ambiguous and ill-defined.

"cA2" and "A2" are distinguishable antibodies.

Even though it has been noted that the requirements under 35 USC 112, first and second paragraphs, for the claimed cA2 antibody have been satisfied in the priority applications, some of which are patented now the examiner has set forth a rejection under 35 USC 112 firs paragraph, for the deposit of the cA2 antibody to clarify the record for the instant application in an effort to clarify the record.

The instant record should indicate the parameters that have satisfied the requirement under 35 USC § 112, second paragraph as well as the enablement requirements under 35 USC 112, first paragraph, for the cA2 antibody.

B) Claims 1, 3-5, 7-12, 14-15, 21, 23-24 and 26-32 are indefinite in the recitation of "TNFα-mediated neoplastic disease" because the metes and bounds of said "TNFα-mediated neoplastic disease" is ill-defined and ambiguous.

Applicant relies upon "TNF-α-related human diseases", including "acute and chronic diseases" and "neoplastic disease", which is characterized as a disease or condition associated with levels of a substance reactive with an anti-TNF antibody to support the recitation of "TNF-α-mediated neoplastic disease", as currently claimed.

Also, the cytokine TNF-α may be related to certain tumors or may be expressed / secreted by certain tumors, neoplastic disease are due to a number of causative agents and etiologies but not mediated or transmitted by TNF-α.

Further, it is noted the earliest priority application USSN 07/670,827, filed 3/18/91, simply discloses "malignant diseases involving TNF-secreting tumors" in the context of as "a disease or condition associated with levels of a substance reactive with an anti-TNF antibody",
while subsequent priority USSNs describe "TNF-secreting tumors or other malignancies involving TNF, such as chronic lymphocytic and/or myelodysplastic syndrome and lymphomas".

There is insufficient characteristics of the nature and targeted "TNFα-mediated neoplastic diseases" to apprise the ordinary artisan of the metes and bounds of the claimed methods.

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06.

5. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.
The specification as originally filed does not provide support for the invention as now claimed:
"TNF-α-mediated neoplastic disease".

Applicant's reliance upon various sections of the instant specification as well as the disclosure of the priority applications USSNs 07/670,827 and 07/943,852 to support the recitation "TNF-α-mediated neoplastic disease" is acknowledged.

However, the recitation of "TNF-α-mediated neoplastic diseases" is not readily apparent either in the pending or priority application.
Applicant relies upon "TNF-α-related human diseases", including "acute and chronic diseases" and "neoplastic disease", which is characterized as a disease or condition associated with levels of a substance reactive with an anti-TNF antibody to support the recitation of "TNF-α-mediated neoplastic disease", as currently claimed.

Also, the cytokine TNF-α may be related to certain tumors or may be expressed / secreted by certain tumors, neoplastic disease are due to a number of causative agents and etiologies but not mediated or transmitted by TNF-α.

The instant claims now recite limitations which were not clearly disclosed in the priority applications as well as the specification as-filed, and would have changed the scope of the priority applications and do change the scope of the instant disclosure as-filed.

Further, neither the priority applications nor the instant application have provides a sufficient description of a representative number of species to represent the entire genus of "TNF-α-mediated neoplastic diseases", as currently claimed.

It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

Therefore, reliance upon the genus of "TNF-α-mediated / related human diseases" and the disclosure of "malignant diseases involving TNF-secreting tumors" text under the heading of TNF-related pathologies does not provide sufficient written description for "TNF-α-mediated neoplastic diseases", as currently claimed.

Also it is noted that the earliest priority application USSN 07/670,827, filed 3/18/91, simply discloses "malignant diseases involving TNF-secreting tumors" in the context of as "a disease or condition associated with levels of a substance reactive with an anti-TNF antibody",
while subsequent priority USSNs describe "TNF-secreting tumors or other malignancies involving TNF, such as chronic lymphocytic and/or myelodysplastic syndrome and lymphomas".

Therefore, the written description of defining TNF-related malignancies has changed in the family of priority documents for this application

Also, it is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Applicant's arguments concerning priority of the instant claims as they would read on similar principles of written description with respect to this new matter rejection under 35 USC 112, first paragraph, drawn to "TNF-α-mediated myelodysplastic syndrome" have not been found persuasive.

The specification as filed does not provide a sufficient written description or set forth the metes and bounds of this phrase. The specification does not provide blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.
Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.
See MPEP 714.02 and 2163.06

7. Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs such as cytokine antagonists can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental and clinical observations associated with the use of anti-TNFα antibodies in the treatment of certain autoimmune diseases accurately reflects the relative ability or efficacy of the claimed therapeutic strategy to treat "TNF-mediated neoplastic diseases" with TNFα-specific antibodies.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.
See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively treat any "TNF-mediated neoplastic disease" by administering anti-TNFα antibodies, including the cA2 specificity. The specification does not teach how to extrapolate data obtained from in vitro and in vivo experimental observations and treatment of certain autoimmune diseases (e.g. rheumatoid arthritis) to the development of effective in vivo human therapeutic methods to any treat any "TNF-mediated neoplastic disease", commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the claimed anti-TNFα antibodies, including the cA2 specificity exemplified in the specification, encompassed by the claims.

Mocellin et al. (Cytokine & Growth Factor Reviews 16: 35 – 53, 2005) reviews tumor necrosis factor, cancer and anticancer therapy, including the use of anti-TNF therapy, including the instant cA2-specific anti-TNF antibodies (see entire document, particularly Section 6.2 Anti-TNF therapy and cancer on page 44). The studies do not support a tumor preventive role of anti-TNF therapy. No direct anticancer activity could be demonstrated in the treatment of hematological malignancies or solid tumors.

Further, it is noted that The Merck Manual of Diagnosis and Therapy, Sixteenth Edition, edited by Beers et al., Merck Research Laboratories, Rahway, NJ, 1992, does not indicate that treatment with anti-TNFα antibodies is an accepted treatment of cancer. See Oncology on pages 1263-1287).

There is insufficient guidance and direction in the specification as filed as to which heart pathologies are being targeted by the claimed methods, nor is there sufficient guidance and direction as to which carcinomas would be targeted by the claimed methods.

There is insufficient objective evidence that therapeutic methods that rely upon anti-TNFα antibodies in the treatment of certain autoimmune diseases, such as rheumatoid arthritis can be extrapolated to predict the ability of such anti-TNFα antibodies, including the cA2 specificity to treat "TNF-mediated neoplastic diseases", commensurate in scope with the claimed invention.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 18 24 (CCPA 1970).

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective anti-cytokine, including anti-TNFα antibodies in the treatment of "TNF-mediated neoplastic diseases", undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for inhibiting "TNF-mediated neoplastic diseases" with anti-TNFα antibodies, including the cA2 specificity.

8. Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the A2 and cA2 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

Affidavits and declarations, such as those under 37 C.F.R. § 1.131 and 37 C.F.R. § 1.132, filed during prosecution of the parent application do not automatically become a part of this application. Where it is desired to rely on an earlier filed affidavit, the applicant should make the remarks of record in the later application and include a copy of the original affidavit filed in the parent application.

As noted previously, given the disclosure and the claims encompassing the instant cA2 antibody set forth in U.S. Patent No. 5,919,452; the conditions for the deposit of biological materials under 35 USC 112, first paragraph, with respect to cA2 appear to have been satisfied.

However, applicant is required to make the record clear exactly what is the scope of the instantly claimed A2 and cA2 antibodies and whether applicant has satisfied the deposit requirements under 35 USC 112, first paragraph, for the claimed A2 and cA2 antibodies.

If applicant is relying upon sequence information to satisfy the deposit of biological materials, i is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific A2 and cA2 antibodies requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences

Applicant's amendments, including the Townsend Declaration under 37 CFR 1.132, filed 12/29/06, have satisfied the deposit requirements under 35 USC 112, first paragraph with respect to the A2 antibody (ATCC PTA-7045).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3-5, 7-10, 12-14, 16-17,19-20 and 22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Verhoef et al. (Leukemia 6: 1268 – 1272, 1992) in view of Le et al. (WO 92/16553) essentially for the reasons of record.

Applicant's arguments, filed 12/29/05, have been fully considered but are not found convincing essentially for the reasons of record.

As indicated above, applicant's assertions concerning priority of the instant claims have been fully considered, but have not been found convincing. Therefore the prior art stands as prior art.

In addition as noted previously, applicant's efforts to argue unexpected results are not found convincing in view of the prior art Le et al. (WO 92/16553), which teaches the same advantages of the cA2 anti-TNF-α antibody as currently claimed.

The following of record is reiterated for applicant's convenience.

Verhoef et al. teach the therapeutic intervention of TNF-α with agents such as anti-TNF- antibodies in the treatment of anemias observed in myelodysplastic syndrome (see entire document, particularly page 1271, column 2, last sentence).

Verhoef et al. differs from the claimed invention by not disclosing the particular anti-TNF- α cA2 specificity.

Le et al. teach the cA2 anti-TNF-α antibody, including the chimeric cA2 anti-TNF- α antibody as well as its therapeutic use in subjects having pathologies and conditions associated with TNF- α (See entire document, including the Summary of the Invention and Detailed Description of the Invention, including page 34, paragraph 1).). Also see pages 34-38 for the well known dosing and modalities of administering therapeutic antibodies of interest to meet the needs of the patients as well as the Examples for affinity constants of prior art cA2-specific antibodies.

Although Verhoef et al. and Le et al. do not disclose humanized and human antibodies per se as therapeutic antibodies, one of ordinary skill in the art at the time the invention was made was motivated to make and use humanized and human antibodies in treating humans, given their well known advantages of their lower immunogenicity when compared to therapeutic antibodies which comprised non-human elements (e.g. murine monoclonal antibodies)

Therefore it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching so Le et al. to those of Verhoef et al. to obtain antagonistic TNF- α-specific antibodies, including those with the cA2 specificity to counter the negative effects of TNF- α in myelodysplastic syndrome. According to Verhoef et al., a person of ordinary skill in the art would have been motivated to administer anti-TNF- α antibodies to counter the involvement of TNF α in the pathogenesis of anemias in myelodysplastic syndrome (See Abstract and Discussion). Le et al. provides for antagonistic anti-TNF-α antibodies, including recombinant antibodies that are less immunogenic than murine monoclonal antibodies in therapeutic modalities involving humans. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

11. It is noted that applicant has a number of copending applications drawn to methods of treating various diseases and conditions with the same cA2 TNF-specific antibodies.

Again, given the history of a number of continuations-in-part, it is not readily apparent whether the claims were subject to restriction and whether the claims are subject to double patenting rejections.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

It is noted that applicant has a number of copending applications drawn to methods of treating various diseases and conditions with the same cA2 TNF-specific antibodies.

Again, given the history of a number of continuations-in-part, it is not readily apparent whether the claims were subject to restriction and whether the claims are subject to double patenting rejections.

Applicant is invited to clarify which applications should be subject to rejections under the judicially created doctrine of obviousness-type double patenting.

Therefore, applicant is notified that the instant application is subject to *provisional* obviousness-type double patenting rejections over copending applications because the conflicting claims have not in fact been patented;

however, such provisional rejections will not be made at this time, given the number of pending applications and the early stage of prosecution.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
March 20, 2006